Amendments to the Specification:

Please replace the paragraph beginning at page 5, line 6 with the following rewritten paragraph:

Figure 5 shows beneficial CDR mutations for anti-cryptic collagen site antibody HUI77. Figure 5A shows a set of primers used to generate random mutations in LCDR3 (SEQ ID NOS:359-367) and HCDR3 (SEQ ID NOS:368-380) of HUI77. Figure 5B shows a set of primers used to generate random mutations in LCDR1a (SEQ ID NOS:312-319), LCDR1b (SEQ ID NOS:320-327), LCDR2 (SEQ ID NOS:328-334), HCDR1 (SEQ ID NOS:335-341), HCDR2a (SEQ ID NOS:342-349) and HCDR2b (SEQ ID NOS:350-357) of HUI77. Figure 5C shows beneficial CDR mutations of the HUI77 antibody.

Please replace the paragraph beginning at page 18, line 1, with the following rewritten paragraph:

An antibody of the invention can have binding activity for a cryptic collagen epitope that is the same as the respective parental mouse antibody. For example, an antibody of the invention having CDRs derived from HUIV26 can have essentially the same binding specificity as the mouse HUIV26 antibody described by Xu et al., Hybridoma 19:375-385 (2000); Xu et al., J. Cell Biol. 154:1069-1079 (2001); and WO 00/40597, ~~each of~~ which is incorporated herein by reference. Similarly, an antibody of the invention having CDRs derived from HUI77 can have essentially the same binding specificity as the mouse HUI77 antibody described by Xu et al., supra, 2000; Xu et al., supra, 2001; and WO 00/40597. Such binding specificity can be tested by the methods disclosed herein, for example, by comparing the activity of an antibody of the invention to the corresponding parental mouse antibody. For example, an antibody of the invention derived from HUIV26 can be compared to a corresponding mouse antibody having the variable region amino acid sequence shown in Figure 2C (SEQ ID NOS:2 and 4). Similarly, an antibody of the invention derived from HUI77 can be compared to a corresponding mouse antibody having the variable region amino acid sequence shown in Figure 3C (SEQ ID NOS:10 and 12). Similar binding specificity can be determined, for example, by competitive binding with the corresponding parental antibody. It is understood that an antibody

of the invention can have essentially the same specificity as the corresponding parental antibody or can have altered specificity so long as the antibody has binding activity for a cryptic collagen epitope.

Please replace the paragraph beginning at page 19, line 9, with the following rewritten paragraph:

Highly specific monoclonal antibodies have been developed that recognize a cryptic domain of human collagen, designated HUIV26 and HUI77 (see Xu et al., Hybridoma 19:375-385 (2000); Xu et al., J. Cell Biol. 154:1069-1079 (2001); WO 00/40597, ~~each of~~ which is incorporated herein by reference). Monoclonal antibody HUIV26 recognizes a cryptic domain of human collagen-IV, and HUI77 recognizes a cryptic domain of human collagen-I and IV that is also common to collagens II, III and V. This cryptic domain(s) is less accessible under most normal physiological conditions but becomes accessible following proteolytic remodeling of the collagen triple helix in vivo. Thus, cryptic collagen epitope(s) can become more accessible during invasive cellular processes. Importantly, the cryptic domain(s) defined by these antibodies was shown to be exposed within the basement membrane of tumor associated angiogenic blood vessels from human tumors including, breast, bladder and melanoma tumors. However, this cryptic domain was less exposed within the vessels or normal tissues tested. Therefore, the antibodies HUIV26 and HUI77 represent important and specific markers of angiogenic blood vessels. These cryptic domain(s) plays an important role in regulating angiogenesis and tumor growth since the monoclonal antibodies HUIV26 and HUI77 potently inhibit angiogensis and human tumor growth in the chick embryo, rat and mouse models following systemic administration (Xu et al., supra, 2001). Thus, these monoclonal antibodies and the antibodies of the invention having specific binding activity for these cryptic collagen site(s) represent a highly potent and effective new therapeutic reagent for the treatment for diseases characterized by aberrant neovascularization.

Please replace the two paragraphs beginning on page 87, line 16 with the following rewritten paragraphs:

Shown in Figures ~~4B~~4C and ~~5B~~5C is a summary of beneficial CDR mutations in the HUIV26 and HUI77 antibodies, respectively. Figure ~~4B~~4C summarizes beneficial single amino acid mutations in heavy chain CDR1, CDR2, and CDR3 and light chain CDR1 and CDR3 of HUIV26. An exemplary HUIV26 variant having a single amino acid substitution is the 12F10Q variant, which exhibited k_{on} of 0.055 and k_{off} of 0.049 as estimated by the fold improvement based on shifts in half-maximal binding obtained from ELISA titrations.

Figure ~~5B~~5C summarizes beneficial single amino acid mutations in heavy chain CDR1, CDR2 and CDR3 and light chain CDR1, CDR2 and CDR3 of HUI77. As can be seen, numerous single amino acid mutations in various CDRs were found to maintain or enhance binding to a cryptic collagen site.

Please replace the paragraph beginning on page 57, line 10 with the following rewritten paragraph:

Methods for measuring the affinity, including association and dissociation rates using surface plasmon resonance are well known in the art and can be found described in, for example, Jönsson and Malmquist, Advances in Biosensors, 2:291-336 (1992) and Wu et al. Proc. Natl. Acad. Sci. USA, 95:6037-6042 (1998). Moreover, one apparatus well known in the art for measuring binding interactions is a ~~BIAcore~~ BIACORE 2000 instrument which is commercially available through Pharmacia Biosensor, (Uppsala, Sweden).

Please replace the paragraph beginning on page 64, line 11 with the following rewritten paragraph:

Formats for measuring association rates in non-equilibrium mixtures include, for example, surface plasmon resonance and evanescent wave instruments. Surface plasmon resonance and evanescent wave technology utilize a ligand or binding polypeptide attached to a biosensor surface and a solution containing either the binding polypeptide or ligand respectively that is passed over the biosensor surface. The change in refractive index of the solution that occurs at the surface of a chip when binding polypeptide associates with ligand can be measured

in a time dependent fashion. For example, surface plasmon resonance is based on the phenomenon which occurs when surface plasmon waves are excited at a metal/liquid interface. Light is directed at, and reflected from, the side of the surface not in contact with sample, and SPR causes a reduction in the reflected light intensity at a specific combination of angle and wavelength. Biomolecular binding events cause changes in the refractive index at the surface layer, which are detected as changes in the SPR signal. The binding event can be either binding association or disassociation between a receptor-ligand pair. The changes in refractive index can be measured essentially instantaneously and therefore allows for determination of the individual components of an affinity constant. More specifically, the method enables accurate measurements of association rates (k_{on}) and disassociation rates (k_{off}). Surface plasmon resonance instruments are available in the art including, for example, the ~~BIAcore~~BIACORE instrument, IBIS system, SPR-CELLIA system, ~~Spreeta~~SPREETA, and Plasmon SPR and evanescent wave technology is available in the Iasys system as described, for example, in Rich and Myszka, Curr. Opin. Biotech. 11:54-61 (2000).

Please replace the paragraph beginning on page 82, line 26 with the following rewritten paragraph:

The variable regions of the HUIV26 and HUI77 antibodies were cloned from hybridomas expressing these mouse monoclonal antibodies and sequenced. Briefly, total mRNA was isolated from the respective mouse hybridoma cells using Oligotex® Direct mRNA Micro kit (Qiagen; Valencia CA). First strand cDNA was synthesized from the mRNA using ~~SuperScript~~SUPERSCRIPT Preamplification System (GibcoBRL/Invitrogen; Carlsbad CA). Antibody variable region sequences were amplified by PCR using a set of 5' primers designed for signal sequences of mouse light chains or heavy chains to pair with single 3' primer to mouse kappa chain constant region for V_L or IgM CH1 region for V_H sequences. The sequences of the 5' primers for the signal peptide of mouse antibody heavy and light chain as well as constant region primers are shown in Figure 1. The 3' primer for mouse kappa light chain constant region (primer 2650; SEQ ID NO:212) corresponds to amino acids 115-123. The 3' primer for mouse IgM CH1 region (primer 2656; SEQ ID NO:213) corresponds to amino acids 121-114. The 3'

primer for mouse IgM CH1 region (primer 2706; SEQ ID NO:214) corresponds to amino acids 131-124.

Please replace the paragraph beginning on page 86, line 3 with the following rewritten paragraph:

The assembled V_L and V_H regions were introduced into a Fab expression vector by mutagenesis. Briefly, the non-biotinylated minus strands were isolated after binding the PCR products to ~~NeutrAvidin-conjugated~~ NEUTRAVIDIN-conjugated magnetic beads and introduced into the Fab expression vector IX-104CSA by hybridization mutagenesis (Kristensson et al., Vaccines 95, pp. 39-43, Cold Spring Harbor Laboratory, Cold Spring Harbor (1995); Kunkel, Proc. Natl. Acad. Sci. USA 82:488-492 (1985); Wu et al., J. Mol. Bio. 294:151-162 (1999)).